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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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11/765,720

06/20/2007

GEROLD SCHULER

106985-5 (2)

8028

27384 7590 09/03/2008  
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EXAMINER

JUEDES, AMY E

ART UNIT

PAPER NUMBER

1644

MAIL DATE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 11/765,720	<b>Applicant(s)</b> SCHULER ET AL.	
	<b>Examiner</b> AMY E. JUEDES	<b>Art Unit</b> 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 29-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 29-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 June 2007 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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**DETAILED ACTION**

1. Applicant's amendment and remarks, filed 6/20/07, are acknowledged.

2. In the remarks filed 6/20/07, Applicant indicates that the original claims have been canceled in favor of new claims 19-22. However, the original claims are numbered 1-28. Thus, the numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 19-22 have been renumbered 29-32.

3. Claims 29-32 are pending and are under examination.

4. The drawings are objected to because the Y axis label is missing for Fig. 4B. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

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which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-32 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A method of suppressing the proliferation of "CD4+ T cells ex vivo or in vivo" comprising "introducing Tr1 like regulatory cells to a composition comprising CD4 T cells" (Claim 29, and dependant claims 30-32).

Applicant indicates that support for the new claims can be found on pages 3-4, 9, and in Example 4 of the specification.

A review of the specification fails to reveal support for the new limitations.

The specification discloses a method of producing Tr-1 like regulatory T cells comprising anergizing CD4+CD25- T cells by contact with CD4+CD25+ T cells. The specification on page 3 discloses that human anergized CD4+CD25- T cells (i.e. Tr1 like regulatory T cells) can suppress proliferation of syngeneic CD4+ T cells. However, this does not provide adequate support for the instant claims which are drawn to suppressing the proliferation of any CD4+ T cell, not just a human syngeneic CD4 T cell, as disclosed on page 3 of the specification. Furthermore, page 3 does not provide adequate support for suppressing CD4 T cells "ex-vivo or in vivo" as recited in the claims. Page 9 of the specification describes the results of Example 4, in which CFSE labeled human CD4+CD25+ T cells were cultured with CD4+CD25- T cells for 48h, followed by separating the two populations. The separated and anergized CD4+CD25- T cells were then used in vitro to inhibit CD4+ T cell proliferation. However, this specific example has a much narrower scope than the instant claims, which encompass suppressing any CD4 T cell either ex-vivo or in vivo with any

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Tr1 like regulatory T cell produced by contact with any CD4+CD25+ T cell. Example 4 of the specification only discloses suppressing human CD4 T cells in vitro with human regulatory T cells that have been anergized with CFSE labeled human CD4+CD25+ T cells for 48h.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 29-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Jonuleit et al., July 15, 2002 (of record).

Jonuleit et al. teach a method of suppressing the proliferation of CD4+ T cells comprising anergizing CD4+CD25- conventional T cells with CD4+CD25+ T cells ex vivo to generate regulatory T cells, and contacting said regulatory T cells ex-vivo with syngeneic CD4+ T cells to suppress their proliferation (see page 256, 258, and Fig. 2A, in particular). Furthermore, the regulatory T cells taught by Jonuleit et al. would inherently be IL-10 producing Tr1-like regulatory T cells, since they have been obtained by a method identical to that of the instant claims.

Thus, the reference clearly anticipates the invention.

8. Claims 29-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Levings et al., J. Immunol., May 2001, as evidenced by Takahata et al., Exp. Hem., 2004.

Levings et al. teach a method of suppressing autologous (i.e. syngeneic) CD4 T cell proliferation comprising contacting said CD4+ T cells with IL-10 producing Tr1 regulatory T cells (see page 5535 and Fig. 6 in particular). Levings et al. also teach producing the Tr1 regulatory T cells by culturing total cord blood CD4+ T cells ex-vivo (see page 5531-5532, in particular). As evidenced by Takahata et al., cord blood CD4+ T cells comprise both CD25+ and CD25 negative subsets (see 623 and

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Fig. 6, in particular). Thus, by culturing total cord blood CD4+ T cells to produce the Tr1 regulatory T cells, Levings et al. have inherently contacted and anergized CD4+CD25- T cells with CD4+CD25+ T cells, as recited in the instant claims.

Thus, the reference clearly anticipates the invention.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 6am - 2pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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